Synthesis and Characterization of Chitosan-Polycaprolactone Blended with Organoclay for Control Release of Doxycycline

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ABSTRACT: In the present research program, chitosan has been mixed with polycaprolactone (PCL) (80 : 20) for using them for control delivery of doxycycline. Organoclay, Cloisite 30B of different concentrations 1, 2.5, and 5% has been blended with the composite. Chitosan is a natural biodegradable polymer where as polycaprolactone is a synthetic biopolymer. The blending of the two polymers has been carried out varying the proportion of nanoclay so that the composite can be a better drug carrier. The blends were characterized by Fourier Transmission Infrared Spectroscopy (FTIR), Scanning Electron Microscopy (SEM), X-ray Diffraction (XRD) analysis. From the FTIR spectra, the various groups present in chitosan and PCL blend were monitored. The homogeneity, morphology, and crystallinity of the blends were ascertained from SEM and XRD data, respectively. The swelling studies have been carried out at different drug loading. Swelling study is an important parameter to predict the diffusion of the drugs from the matrix. The kinetics of the drug delivery system has been systematically studied. Drug release kinetics was analyzed by plotting the cumulative release data versus time by fitting to an exponential equation which indicated the non-Fickian type of kinetics. The drug release was investigated at different pH medium, and it was found that the drug release depends upon the pH medium as well as the nature of matrix. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 118: 3167–3175, 2010

Key words: polycaprolactone; chitosan; doxycycline; blending; drug delivery; kinetics

INTRODUCTION

Carrier-mediated drug delivery has emerged as a powerful methodology for the treatment of various pathologies. The therapeutic index of traditional and novel drugs is enhanced via the increase of specificity due to targeting of drugs to a particular tissue, cell or intracellular compartment, the control over release kinetics, the protection of the active agent or a combination of the above.[1] Polymer composites were proposed as drug carriers over 30 years ago and have received growing attention since, mainly due to their stability, enhanced loading capabilities, and control over physicochemical properties.[2,3] In addition to systemic administration, localized drug release may be achieved using macroscopic drug depots close to the target site. In recent years, biodegradable polymers have attracted attention of researchers to be used as carriers for drug delivery systems.[4–6]

Chitosan (CS) is a biopolymer that has received great attention in a variety of applications because of their biodegradability and biocompatibility.[7] It is derived from chitin, which is the second most abundant biomass on earth next to cellulose and is available from waste products in the shellfish industry. Because of its excellent film-forming property, chitosan can be used effectively as a film-forming material to carry active ingredients such as mineral or vitamin for food packaging applications,[8] a hydrophilic or hydrophobic drugs for drug delivery applications.[9] Chitosan is a cationic biopolymer that is bioadhesive, biocompatible, and biodegradable. These unique properties make it an attractive carrier for biomedical applications. Of late, chitosan has been widely applied in biomedical fields as a carrier for drug delivery, wound dressing, etc.[10] Since chitosan is already known as a biocompatible, biodegradable, and almost nontoxic material, it has been widely used in pharmaceutical research and industry as a carrier for drug delivery and as biomedical material.[11] Orally administered as well as implantable delivery systems containing chitosan as a drug carrier have been prepared to effect sustained release of the drug.[12,13] Modulation of drug release has been achieved by drug–chitosan complexation involving ionic[14–16] or covalent interactions.[17,18] While the focus for ionic interactions of chitosan involves the amino groups of its glucosamine

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residues, covalent interactions often involve other sites as well (e.g., the CH_2OH moieties). Despite the advantages stated in the previous section, primarily chitosan lacks the mechanical properties required for being an ideal matrix material. For example, the tensile strength of an articular cartilage is around 27 MPa,[19] whereas chitosan has shown a strength of only 5–7 MPa, in the wet state.[20] The rationale for combining chitosan with other polymers has been diverse and application-specific.

Polycaprolactone (PCL), semi-crystalline, and resorbable aliphatic polyester has found various biomedical applications such as sutures, drug delivery systems, and scaffolds in tissue engineering, due to its soft- and hard-tissue compatible properties and biodegradation characteristic. It is an FDA approved biomaterial, currently used in drug delivery and sutures.[21] Its low melting point (60°C) allows easy processing and it is biodegradable by hydrolysis. Although PCL has been widely used as a matrix material, its applications are frequently limited by several drawbacks including limited bio-regulatory activity, hydrophobicity,[22] neutral charge distribution, slow rate of degradation, and acidic degradation products. In addition, like other synthetic biodegradable polyesters, PCL is costly and therefore its applications are restricted to some extent. Numerous efforts have been focused on overcoming these drawbacks. One of the common strategies is to blend PCL with other natural biopolymers, including starch, zein, cellulose, and chitosan.[23,24] Application of PCL for controlled drug delivery systems has a draw back of slow degradation rate in vivo due to its high crystallinity and hydrophobicity. It has been reported the biodegradability of PCL can be enhanced by copolymerizing[25–27] or blending with a variety of other polymers.[28] Enhancement of hydrophilicity of PCL has been achieved by the chemical blending with natural polymer such as chitosan.[29,30]

Blending two polymers is an effective way to develop new material with combinations of properties not possessed by individual polymers. The wide range of physico-chemical properties and processibility of synthetic polymers can integrate with good biocompatibilities and biological interactions of natural polymers by blending synthetic polymers with natural polymers. Polycaprolactone (PCL) is a kind of biodegradable aliphatic polyester with good biocompatibility. And it is an ideal matrix material for its valuable properties such as non-toxicity for organism, gradual resorption after implantation, and good mechanical properties.[31] Chitosan has many usages such as sorbent in waste water treatment, wound addressing, and drug carrier in pharmaceutical applications because it has been proven to be biodegradable, biocompatible, nonantigenic, nontoxic, and biofunctional.[32] Furthermore, the positive charged chitosan is easy to interact with negative charged glycosaminoglycans in the extracellular matrix. Since the properties of PCL and chitosan are complementary, it is possible that blending the two polymers will give composite owning properties of ideal matrix material such as biocompatibility, biodegradability, and the ability to tissue development.[33] Several studies have been conducted to make PCL-CS composite. Sarasam et al. prepared PCL-CS composite membranes and porous scaffolds in a unique solution of acetic acid.[34]

A recent survey of the literature reveals that chitosan-PCL blended with cloisite 30B has not been used as a carrier for controlled drug delivery systems. The composite has been blended with different amounts of cloiste 30B to be used for drug delivery. Clay minerals are widely used materials in drug products both as excipients and active agents. Montmorillonite (MMT) can provide mucoadhesive capability for the nanoparticle to cross the gastrointestinal (GI) barrier.[35] MMT is also a potent detoxifier, which belongs to the structural family of 2 : 1 phyllosilicate. MMT could absorb dietary toxins, bacterial toxins associated with gastrointestinal disturbance, hydrogen ions in acidosis, and metabolic toxins such as steroidal metabolites associated with pregnancy.[36]

Hombreiro Perez et al. has been reported the controlled release of drug nifedipine from PCL microparticles[37] and according to Sinha et al. chitosan was also used for the controlled release of various drugs.[38] But no one has done the controlled release of drug from chitosan/PCL composites blended with C30B. So in the present research program, we are using chitosan-PCL composites, both of which are biodegradable, and biocompatible has been blended with Cloisite 30B which is organically modified sodium in MMT with quaternary ammonium salt (1, 2.5, and 5%) for the controlled release of doxycyline. The blends have been characterized using FTIR, Scanning Electron Microscopy (SEM), and X-ray Diffraction (XRD). This nanocomposites (1% Cloisite 30B) has been compounded with doxycycline and the control release of the drug doxycycline has been evaluated. The swelling kinetics as well as the drug delivery systems using doxycycline has also been studied at different pH. 7.4 pH was used as alkaline medium and 3.4 pH was used as acidic medium for evaluating the drug release. The structure of doxocycline is presented in Figure 1.

EXPERIMENTAL

Materials

Chitosan (CS) (degree of deacetylation = 95% determined by ^1H NMR) was purchased from India Sea Food, and Polycaprolactone (PCL), under the

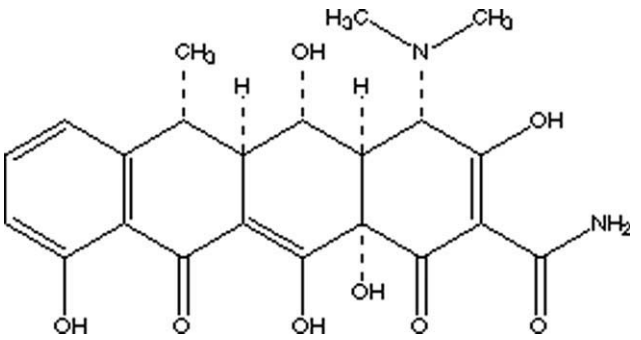

Figure 1 Structure of doxycycline.

commercial name of CAPA 680, was purchased from Solvay Interox Ltd., U.K. Cloisite 30B was procured from Southern Clay Products, Austin, Texas. Doxycycline was received as gift sample from Ranbaxy, India. Acetic acid, NaH_2 PO_4, NaOH, and other chemicals were used as analytical grade and purchased from Sigma Aldrich Company.

Synthesis of chitosan/PCL nanocomposites

Chitosan was dissolved in 0.5 *M* acetic acid and PCL in glacial acetic acid. To prepare sterile 1% (w/v) chitosan solutions, chitosan suspension in water was first autoclaved (at 121°C in a wet cycle for 20 min) and then dissolved by adding acetic acid equivalent to 0.5 *M* in a sterile laminar flow hood. To get chitosan / PCL (80 : 20) ratio, 4 mL of 1% chitosan solution was added to 10 mL of 0.1% PCL solution. The mixtures were stirred at room temperature for 2 h to obtain homogeneous solutions. Calculated amount of C30B was added to this slurry (1, 2.5, and 5%). The mixture was stirred for 8 h at room temperature till a homogenate composite is formed.

Drug loading

Required amount of chitosan- PCL (80 : 20) and nanoclay 1% was taken in 5 mL of acetic acid. The mixture was continuously stirred with a mechanical stirrer. Doxycycline of different loadings, i.e., 10, 20, 30, 40, and 50 wt % were then added to the above mixture and stirred for 1 h and then the composites were kept at room temperature for drying.

Dissolution experiments

Dissolution experiments were performed at 37°C using the dissolution tester (Disso test, Lab India, Mumbai, India) equipped with six paddles at a paddle speed of 100 rpm. About 900 mL of phosphate buffer solution (pH 3.4 and 7.4) was used as the dissolution media to stimulate gastrointestinal tract (GIT) conditions. A 5 mL aliquot was used each time for analyzing the doxycycline content at a fixed time interval. The dissolution media was replenished with a fresh stock solution. The amount of doxycycline released was analyzed using a UV spectrophotometer (Systronics, India) at the λ_{max} value of 270 nm.

CHARACTERIZATION

Fourier transmission infra red spectroscopy

The Fourier Transmission Infrared Spectroscopy (FTIR) spectrum of the chitosan-PCL blends was obtained using a BIORAD-FTS-7PC type FTIR spectrophotometer.

X-ray diffraction

The change in gallery height of the blend was investigated by WAXD experiments, which were carried out using a X-ray diffractometer (BEDE D-3 system) with Cu Kα radiation at a generator voltage of 40 kV and a generator current of 100 mA. Samples were scanned from $2\Theta = 1–10°$ at a scanning rate of 2°/min.

Scanning electron microscopy

The blending of the chitosan-PCL nanocomposites containing different concentrations was characterized using SEM (440, Leica Cambridge, Cambridge, UK). The powdered specimens were placed on the Cambridge standard aluminum specimen mounts (pin type) with double-sided adhesive electrically conductive carbon tape (SPI Supplies, West Chester, PA). The specimen mounts were then coated with 60% Gold and 40% Palladium for 30 s with 45 mA current in a sputter coater (Desk II, Denton Vacuum, Moorestown, NJ). The coated specimens were then observed on the SEM using an accelerating voltage of 20 kV at a tilt angle of 30° to observe the microstructure of the chitosan-PCL composite blends.

Swelling studies

Water absorption of the polymer-drug conjugates was measured following ASTM D 570-81. The samples were preconditioned at 50°C for 24 h and then cooled in a desiccator before being weighed. The preconditioned samples were submerged in distilled water at 25°C for 24 h. The samples were removed and dried with a paper towel before weighing. Water absorption was calculated as a percentage of initial weight. The soluble material loss was checked by weighting the specimens after drying them in an oven at 50°C for another 24 h. The total water absorption for 24 h was calculated including the

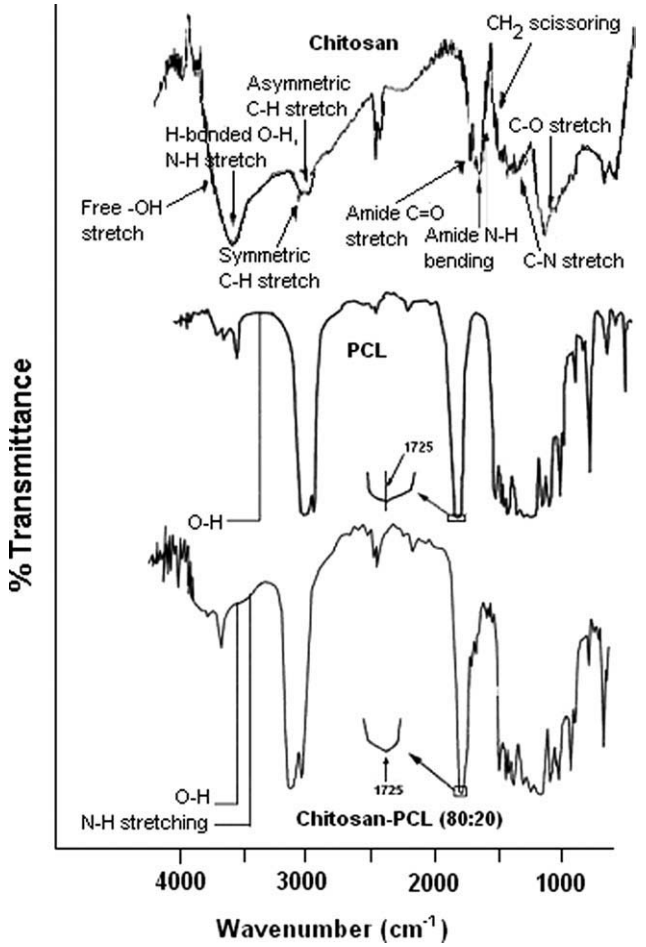

Figure 2 FTIR spectra of chitosan (CS), polycaprolactone (PCL), and chitosan-polycaprolactone (CS-PCL) blend.

soluble material loss

$$\% \text{ Swelling} = \frac{W_1 - W_2}{W_2} \times 100$$

Where, W_1 = weight of swollen composite after 24 h, W_2 = weight of dry composite.

RESULTS AND DISCUSSION

Fourier transmission infra red spectroscopy

Figure 2 shows the FTIR spectra of chitosan (CS), polycaprolactone (PCL), and chitosan-polycaprolactone (CS-PCL) blend. Chitosan is an amino glucose characterized by a small proportion of amide groups via an amide linkage with acetic acid. In the IR spectrum, powder chitosan exhibited a broad peak at 3431 cm^{-1}, which is assigned to the N—H and hydrogen bonded O—H stretch vibrational frequencies, while a sharp (shoulder) peak at 3610 cm^{-1} is that of free O—H bond stretch of glucopyranose units.[39] Further, in the C—H stretch region of FTIR spectrum, the higher the asymmetric and the lower intensity peak at 2857 cm^{-1} is assigned to the symmetric modes of CH_2. In addition, the characteristic band due to CH_2 scissoring, which usually occurs at 1465 cm^{-1} was also present in the sample. Since the grade of chitosan used in the present study was ≥90% deacetylated, an amide bond peak was present in the spectra and the C=O stretch of amide bond was observed at 1661 cm^{-1}. The peaks at 1550 and 1599 cm^{-1} were assigned to strong N—H bending vibrations of secondary amide, which usually occur in the range of 1640– 1550 cm^{-1} as strong band. The IR spectra shows the characteristic peaks of both polymers, i.e., chitosan and PCL (3300–3700, 1725, 852–1480, and 720 cm^{-1}). Furthermore, the IR spectra of chitosan/PCL (10 wt %) produced peaks between 3200 and 3700 cm^{-1}, which were much more intense than the stretching absorbance at 3000–3600 cm^{-1} observed in the absence of chitosan. Additionally, the spectrum in Figure 2 identifies differences in absorbance intensity at 1650 cm^{-1} (primary amide, secondary amide) and 1590 cm^{-1} (non-acylated primary amide).

X-ray diffraction analysis

The XRD patterns of closite 30B along with chitosan/PCL/30B nanocomposites are furnished in Figure 3. From the figure, it is ascertained that the peak corresponding to the basal spacing of the organoclay appears at 4.74 A° with the corresponding (d_{001}) spacing 1.9 nm. For the 1 wt % 30B nanocomposites, we did not see any noticeable peaks of 30B in the low angle range, and this confirmed the exfoliated structure of silicate layers of 30B in the PCL matrix after the mixing. For 2.5 wt % 30B hybrids, a broad peak at 2. 4.6 A° and for 5 wt % a peak at 3.02 A°, much lower than that of closite 30B, was observed, indicating that intercalation of 30B occurred together with some exfoliation. The results in Figure 3 show that intercalation and/or exfoliation of closite 30B

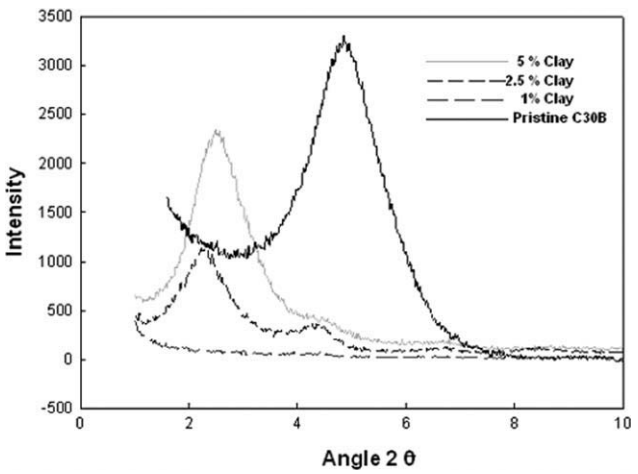

Figure 3 X-ray diffraction patterns of (a) pristine C30B, (b) CS-PCL (80 : 20) 1% clay, (c) CS-PCL (80 : 20) 2.5% clay, (d) CS-PCL (80 : 20) 5% clay.

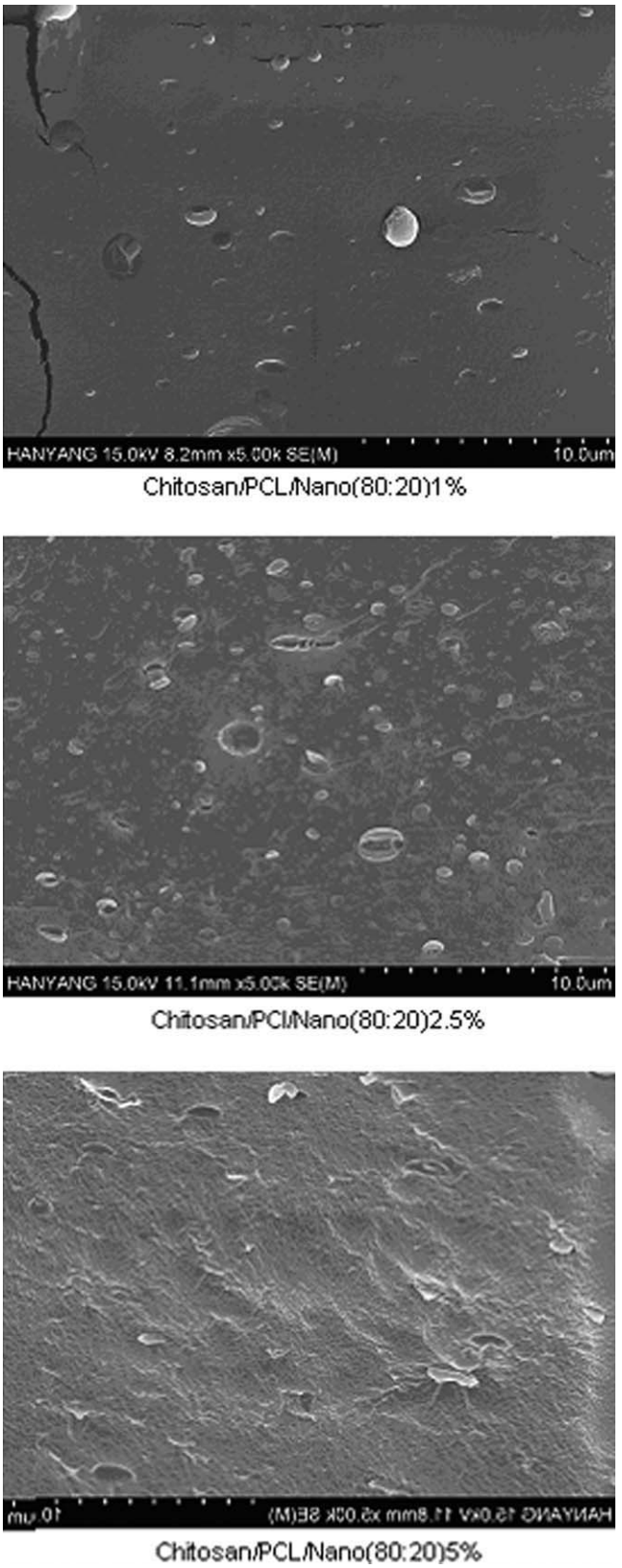

Figure 4 Scanning electron microscope of CS-PCL nanocomposites. Top: CS-PCL (80 : 20) 1% clay, Middle: CS-PCL (80 : 20) 2.5% clay, and Bottom: CS-PCL (80 : 20) 5% clay.

could be accomplished by mixing in an internal mixer. In summary, during the mixing process of the polymer matrix and organoclay, the fracturing process of the organoclay particles takes place first; that is, external platelets are subjected to dynamic high shear forces that ultimately cause their delamination from the stack of layers building the organoclay particles, and then an onion-like delamination process continues to disperse the platelets of silicate into the polymer matrix.[40,41] In the chitosan/PCL/30B nanocomposites, these two steps are also presumed to have taken place.

Scanning electron microscopy

SEM has been employed for the observation of the surface morphology of the different chitosan/PCL nanocomposites. The microstructure obtained by SEM for the chitosan/PCL nanocomposites prepared by mixing, showed that PCL nanoparticles (with irregular forms) are relatively well dispersed in the chitosan matrix. Figure 4 shows that chitosan/PCL nanocomposites is homogenous at low concentration 3% nano, 5% nano. As the concentration of the nanoclay increases from 1% to 5% the homogeneity of the surfaces increases because of the intercalation of the nanoparticles along the polymer matrix. This might enhance the surface modification.[42]

Swelling studies

The swelling behavior of any polymer network depends upon the nature of the polymer, polymer solvent compatibility, and degree of cross-linking. However, in the case of ionic networks, swelling behavior depends upon mass transfer limitations, ion exchange, and ionic interaction.[43] Swelling studies are important to understand the drug release

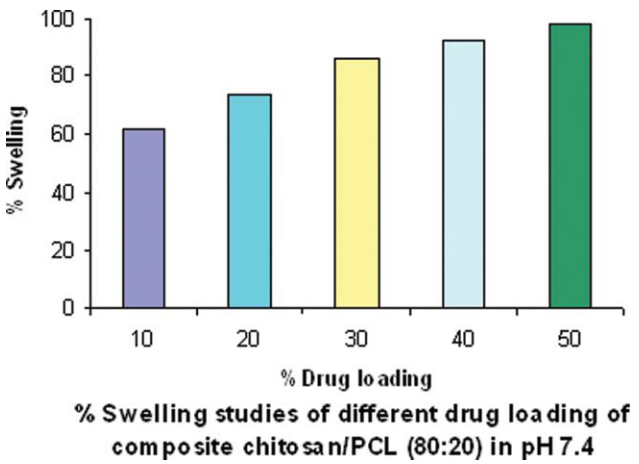

Figure 5 Water absorption of the CS-PCL -nanocomposites with different percentage of drug loadings. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

characteristics of the polymer drug conjugate. It depends upon the nature and extent of interaction between solvent molecules and polymer chains in addition to porosity of the polymer and the nature of hydrophilic groups present on the polymer. Here the percentage of swelling increases with increase in the percentage of drug loading in chitosan/PCL nanocomposites (see Fig. 5).

IN VITRO DRUG RELEASE

The drug delivery system was developed for the purpose of bringing, up taking, retaining, releasing, activating, localizing, and targeting the drugs at the right time period, dose, and place.[44] The biodegradable polymer can contribute largely to this technology by adding its own characters to the drugs. In this connection, some biodegradable polymers such as PLA, PCL, etc., are commonly used as these polymers can be prepared in the moderate conditions, has a similar stiffness of the body and has an appropriate biodegradability and low crystallinity enough to be mixed well with many kinds of drug.[45] There are some formulations for the drug delivery systems, for, e.g., films, gels, porous matrices, microcapsules, micro spheres, nanoparticles, polymeric micelles, and polymer-linked drugs. The physical interactions are usually preferred for binding of the drug to the polymer avoiding damage to the molecular structure of the drug unless it will lead to the loss of bioactivity.[46]

Although, the drug delivery system (DDS) concept is not new, great progress has recently been made in the treatment of a variety of diseases. Targeting delivery of drugs to the diseased lesions is one of the most important aspects of DDS. To convey a sufficient dose of drug to the lesion, suitable carriers of drugs are needed. Nano and microparticle carriers have important potential applications for the administration of therapeutic molecules controlled drug delivery technology represents one of the frontier areas of science, which involves multidisciplinary scientific approach, contributing to human health care. These delivery systems offer numerous advantages compared to conventional dosage forms, which include improved efficacy, reduced toxicity, and improved patient compliance and convenience. Such systems often use macromolecules as carriers for the drugs. By doing so, treatments that would not otherwise be possible are now in conventional use. This field of pharmaceutical technology has grown and diversified rapidly in recent years.

Effect of pH

To investigate the effect of pH on the swelling of composite chitosan/PCL/nano (80 : 20) 1%, we have

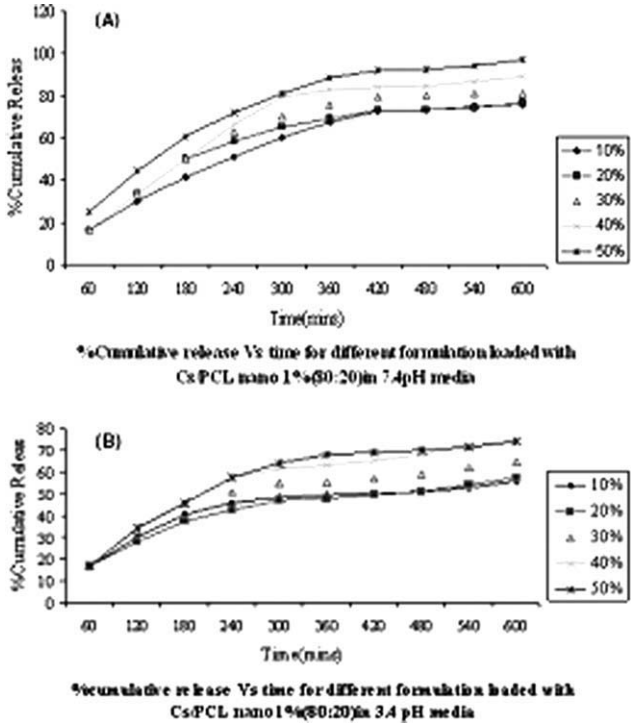

Figure 6 Percentage of cumulative release versus time for different formulation loaded with CS-PCL (80 : 20) nanocomposites in pH 7.4 and pH 3.4 media.

measured the percentage of cumulative release in both pH 3.4 and 7.4 media. Cumulative release data presented in Figure 6 indicate that by increasing the pH from 3.4 to 7.4, a considerable increase in the cumulative release is observed for all composites. From Figure 7(a,b), it is seen that the 50% drug-polymer composites have shown longer drug release rates than the other composites. Thus, drug release depends upon the nature of the polymer matrix as well as pH of the media. This suggests that the drugs in the blend can be used to be suitable for the basic environment of the large intestine, colon, and rectal mucosa for which there are different emptying times.

Effect of time

Interestingly, doxycycline is being released more rapidly at pH 7.4 than at pH 3.4, the release half times t_{50} (time required for releasing 50 wt % of drug) for 10, 20, 30, 40 , 50% drug loading are 2.05, 2.08, 3.0, 3.01, and 4.0 h at pH 7.4, and 3.0, 3.05, 6.0, 7.0, and 8.0 h at pH 3.4, respectively are shown in Figure 8(a,b). More than 80 wt % doxycycline is released from composites at pH 7.4 within 8 h, whereas less than 44 wt % of the drug is released at pH 3.4 within 4 h. This suggests that the drugs in the composites can be used to be suitable for the basic environment, further the electrostatic interaction of composites is more easily broken at pH 7.4 than

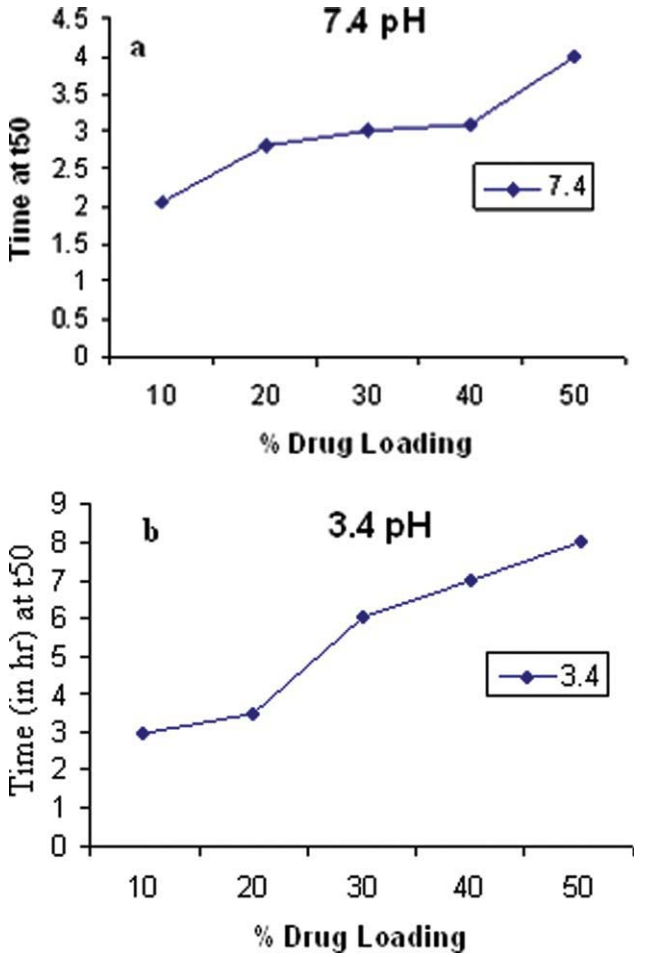

Figure 7 Drug release at time t50 versus drug loading in CS-PCL (80 : 20) nanocomposites at (a) pH 7.4 and (b) pH 3.4.

at pH 3.4, leading to doxycycline being released more rapidly at pH 7.4 than 3.4.

Effect of drug loading

Figure 7 displays the release profiles of drug from composites at different amounts of drug loadings. Release data show that formulations containing highest amount of drug (50%) displayed fast and higher release rates than those formulations containing a small amount of drug loading. The release rate becomes quite slower at the lower amount of drug in the matrix, due to the availability of more free void spaces through which a lesser number of drug molecules could transport.

DRUG RELEASE KINETICS

Drug release mechanism from matrices

From time to time, various authors have proposed several types of drug release mechanisms from matrices. It has been proposed that drug release from matrices usually implies water penetration in the matrix, hydration, swelling, diffusion of the dissolved drug (polymer hydro fusion), and/or the erosion of the gelatinous layer. Several kinetics models relating to the drug release from matrices, selected from the most important mathematical models, are described over here. However, it is worth mention that the release mechanism of a drug would depend on the dosage from selected, pH, nature of the drug, and, of course, the polymer used.

(i). Zero-order kinetics.[47]

$$W = k_1 t \tag{1}$$

(ii). First-order kinetics.[47,48]

$$\ln(100 - W) = \ln\ 100 - k_2 t \tag{2}$$

(iii). Hixon-Crowel's cube-root equation (erosin model).[48]

$$(100 - W)^{1/3} = 100^{1/3} - k_3 t \tag{3}$$

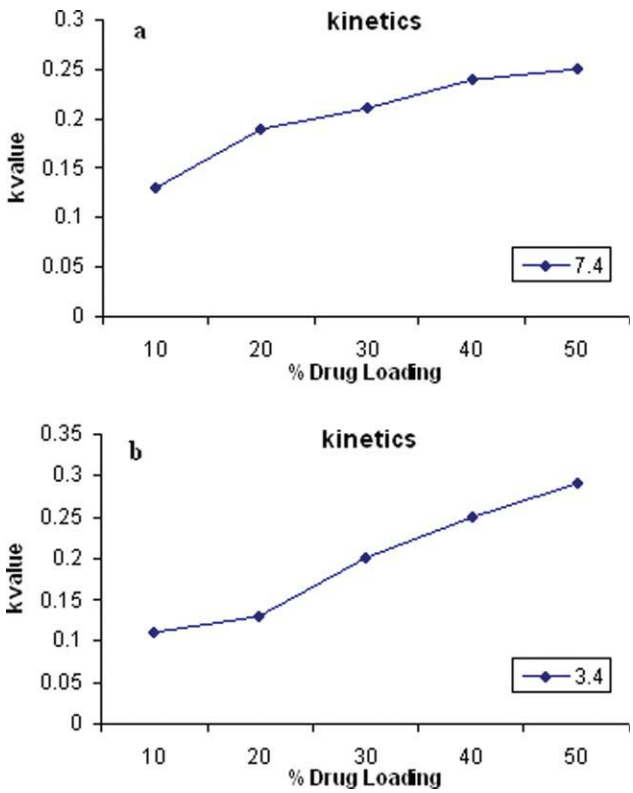

Figure 8 Values of K versus percentage of drug loading in CS-PCL (80 : 20) nanocomposites at (a) pH 7.4 and (b) pH 3.4.

TABLE I
Release Kinetic Parameters of Different Formulations at pH 7.4 and pH 3.4

	k		n		Co-ordination-coefficient, R	
Sample code (wt %)	pH 7.4	pH 3.4	pH 7.4	pH 3.4	pH 7.4	pH 3.4
10	0.13	0.11	1.11	1.35	0.9725	0.9308
20	0.19	0.13	1.25	0.83	0.9687	0.9916
30	0.21	0.20	0.96	1.5	0.9882	0.9654
40	0.24	0.25	1.6	1.33	0.9656	0.9306
50	0.25	0.29	1.02	0.73	0.9723	0.9912

(iv). Higuchi's square root of time equation (diffusion model).[49]

$$W = k_4 t \tag{4}$$

(v). Power law equation (diffusion/ relaxation model).[50]

$$M_t/M_\infty = k_5 t^n \tag{5}$$

M_t/M_∞ is the fractional drug release into dissolution medium and k_5 is a constant incorporating the structural and geometric characteristics of the tablet. The term 'n' is the diffusional constant that characterizes the drug release transport mechanism. When $n = 0.5$, the drug diffuses through and is release from the polymeric matrix with a quasi-Fickian diffusion mechanism. For $n > 0.5$, an anomalous, non-Fickian drug diffusion occurs. When $n = 1$, a non-Fickian, Case II or zero-order release kinetics could be observed.

Drug release kinetics was analyzed by plotting the cumulative release data versus time by fitting to an exponential equation of the type as represented below.[47]

$$M_t/M_\infty = kt^n$$

Here, M_t/M_∞ represents the fractional drug release at time t, k is a constant characteristic of the drug-polymer system, and n is an empirical parameter characterizing the release mechanism. Using the least squares procedure, we have estimated the values of n and k for all the five formulations and these data are given in Table I. The values of k and n have shown a dependence on the, percentage of drug loading and polymer content of the matrix. Values of n for composites prepared by varying the amounts of drug containing 10, 20, and 30 wt % and keeping PCL (20%) and chitosan (80%) constant, ranged from 0.57 to 0.88 suggesting shift of drug transport from Fickian to anomalous type. However, the drug-loaded composites exhibited n values ranging from 0.96–1.57 (see Table I), indicating a shift from erosion type release to a swelling controlled, non-Fickian type mechanism. The value of n more than 1 has also been recently reported.[49,50] This may be due to a reduction in the regions of low micro viscosity inside the matrix and closure of microcavities during the swollen state of the polymer. Similar findings have been found elsewhere, wherein the effect of different polymer ratios on dissolution kinetics was investigated.[48,51]

CONCLUSIONS

Chitosan is a natural biodegradable polymer where as polycaprolactone is a synthetic biopolymer. The blending of the two composites has been blended with Cloisite 30B were prepared and characterized has been carried out so that the composite can be a better drug carrier. From the FTIR spectra, the different pendant groups present in the composites have been ascertained. The morphology as well as the compatibility of the blends has been studied using SEM and XRD methods. From these studies the homogeneity of the blends has been predicted. Swelling study is an important parameter to predict the diffusion of the drugs from the matrix. The percentage of swelling increases with increase in the percentage of drug loading. The drug release depends upon the nature of the polymer matrix as well as pH of the media. The kinetics of the drug release has been investigated. The values of k and n have been computed. Based on the values of n non-Fickian kinetics has been predicted.

References

1. Swain, S. N.; Rao, K. K.; Nayak, P. L. Polym Int 2005, 54, 739.
2. Nanda, P. K.; Rao, K. K.; Nayak, P. L. J Appl Polym Sci 2007, 103, 31.
3. Nanda, P. K.; Rao, K. K.; Nayak, P. L. Polym Plast Technol Eng 2007, 46, 207.
4. Pathak, C. P.; Sawhney, A. S.; Hubbell, J. A. J Am Chem Soc 1992, 114, 8311.
5. Lambert, G.; Fattal, E.; Couvreur, P. Adv Drug Deliv Rev 2001, 47, 99.

6. Mcallister, K.; Sanzani, P.; Adam, M.; Rubinstein, M. J Am Chem Soc 2002, 124, 15198.
7. Ravi Kumar, M. N. V. React Funct Polym 2000, 46, 1.
8. Muzzarelli, R. A. A. Adv Polym Sci 2005, 186, 151.
9. Senel, S.; Ikinci, G.; Kas, S. Int J Pharm 2000, 193, 197.
10. Shu, X. Z.; Zhu, K. J. Int J Pharm 2000, 201, 51.
11. Muzzarelli, R. A. A. Chitin. Pergamon: Oxford, 1977, chapter 3.
12. Vasudev, S. C.; Chandy, T.; Sharma, C. P. Biomaterials 1997, 18, 375.
13. Park, I. K.; Kim, T. H.; Park, Y. H.; Shin, B. A.; Choi, E. S.; Chowdhury, E. H. J Controlled Release 2001, 76, 349.
14. Agnihotri, S. A.; Aminabhavi, T. M. J Controlled Release 2004, 96, 245.
15. Shiraishi, S.; Imai, T.; Otagiri, M. J Controlled Release 1993, 25, 217.
16. Imai, T.; Shiraishi, S.; Saito, H.; Otagiri, M. Int J Pharm 1991, 67, 11.
17. Sabnis, S. S.; Rege, P.; Block, L. H. Pharm Dev Technol 1997, 2, 243.
18. Sanzgiri, Y.; Blanton, C. D.; Gallo, J. M. Pharm Res 1990, 7, 418.
19. Black, J.; Hastings, G. Handbook of Biomaterials Properties; Chapman and Hall, 1998.
20. Cheng, M. Y.; Deng, J. U.; Yang, F.; Gong, Y. D.; Zhao, N. M.; Zhang, X. F. Biomaterials 2003, 24, 2871.
21. Wise, D. L. Encyclopedic Handbook of Biomaterials and Bioengineering Part A: Materials; Marcel Dekker: New York, 1995.
22. Ha, J. H.; Kim, S.; Han, S. Y.; Lee, Y. M.; Kang, I. K.; Cho, C. S. J Controlled Release 1997, 49, 2531.
23. Koenig, M.; Huang, S. Polymer 1995, 36, 1877.
24. Olabarrieta, D.; Forsstrom, U.; Gedde, M. Polymer 2001, 42, 4401.
25. Allen, C.; Han, J.; Maysiger, D.; Eisenberg, A. J Controlled Release 2000, 63, 275.
26. Cai, Q.; Bei, J.; Wang, S. J Biomater Sci 2000, 11, 273.
27. Paul, D. R.; Newman, S. Polym Blends. Academic Press: New York, 1978, Vol. 2, pp 35–89.
28. Hubbell, D. S.; Cooper, S. L. J Appl Polym Sci 1978, 21, 3035.
29. Zhu, K. J.; Xiangzhon, L.; Shilin, L. Y. J Appl Polym Sci 1990, 39, 1.
30. Cohn, D.; Younes, H. J Biomed Mater Res 1988, 22, 993.
31. Zhang, Y.; Zhang, M. J Biomed Mater Res 2001, 55, 304.
32. Khor, E.; Lim, L. Y. Biomaterials 2003, 24, 2339.
33. Liu, X.; Ma, P. X. Ann Biomed Eng 2004, 32, 477.
34. Sarasam, A.; Madihally, S. V. Biomaterials 2005, 26, 55.
35. Krishna Rao, K. S. V.; Vijay Kumar Naidu, B.; Subha, M. C. S.; Sairam, M.; Aminabhavi, T. M. Carbohydr Polym 2006, 66, 333.
36. Forni, F.; Lannuccelli, V.; Coppi, G.; Bernabei, M. T. Arch Pharm 1989, 322, 789.
37. Sunder, M.; Ramesh Babu, N.; Ram Kumar, K.; Sampath Kumar, T. S. Trends Biomater Artif Organs 2005, 18, 213.
38. Sinha, V. R.; Singla, A. K.; Wadhawan, S.; Kaushik, R.; Kumria, R.; Bansal, K.; Dhawan, S. Int J Pharm 2004, 274, 1.
39. Perez, M. H.; Zinutti, C.; Lamprecht, A.; Ubrich, N.; Astier, A.; Hoffman, M.; Bodmeier, R.; Maincent, P. J Controlled Release 2000, 65, 429.
40. Nishimura, S.; Kohgo, O.; Kurita, K. Macromolecules 1991, 24, 4745.
41. Detchprohm, S.; Aoi, K.; Okada, M. Macromol Chem Phys 2001, 202, 3560.
42. Yang, G. L.; Feng Zhaang, G. L. J Membr Sci 1999, 161, 31.
43. Frank, S.; Lauterbur, P. C. Nature 1993, 363, 334.
44. Langer, R. Science 1990, 249, 1527.
45. Lewis, D. H. Controlled release of bioactive agents from lactide/glycolide polymers, Biodegradable Polymers as Drug Delivery Systems. Chasin M, Langer R, Eds., Marcel Dekker: New York, 1990, pp 1–8.
46. Heller, J.; Robinson, J.; Lee, J. R. Controlled Drug Delivery Fundamentals and Applications; Marcel Dekker: New York, 1987; pp 139–212.
47. Xu, G. J.; Sunada, H. Chem Pharm Pharm Bull 1995, 43, 483.
48. Ritger, R. L.; Peppas, N. A. J Controlled Release 1987, 5, 37.
49. Higuchi, T. J Pharm Sci 1963, 52, 1145.
50. Kulkarni, A. R.; Soppimath, K. S.; Aminabhavi, T. M. Pharm Acta 1999, 74, 29.
51. Lyu, S. P.; Sparer, R.; Hobot, C.; Dang, K. J Controlled Release 2005, 102, 679.